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(54) Title of the Invention: Capsule Coating Composition

(21) Application No.: Hei 1[1989]-147,512
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(72) Inventor: Kenji Numata
9-6 Ushitashin-machi 4-chome, Higashi-ku,
Hiroshima-shi, Hiroshima-ken
(71) Applicant: Kotobuki Academy K.K.
9-6 Ushitashin-machi 4-chome, Higashi-ku,
Hiroshima-shi, Hiroshima-ken
(74) Agent: Takashi Miyara, Patent Attorney (and 1 other)

SPECIFICATION

1. Title of the invention: Capsule Coating Composition

2. Claims

(1) A capsule coating composition, characterized in that a plant extract having flavoring properties and anti-spoiling properties is contained in the capsule coating agent.

(2) The capsule coating composition according to claim 1, wherein an extract which is extracted from a plant of the Perilla family is used as the essential component in the plant extract.

(3) The capsule coating composition according to claim 1, in which the plant extract is contained at 2-40 wt% in the capsule coating agent.

3. Detailed description of the invention

(Field of industrial utilization)

The present invention relates to a capsule coating composition, characterized in that spoiling resistance and flavoring are provided, without using synthetic preservatives, by including a natural plant extract in the capsule coating agent.

(Prior art)

In the past, in order to maintain stability in soft capsule preparations for drugs, cosmetics, health foods and other products, synthetic preservatives (such as p-hydroxybenzoic acid ethyl ester preservatives) have been used. A flavoring has also been produced by including other synthetic flavorings.

In addition, because microcapsule preparations are composed primarily of petroleum-based elements, they are inappropriate for long-term [slow-release] medication or foodstuffs.

There have been many inventions related to conventional capsule preparations, which provide improved solubility, gel firmness or adhesive strength, or provide coloration in the coating. For example, with the gelatin soft capsule agent coating described in Japanese Unexamined Patent Application No. Sho 63[1988]-264,519, an invention is disclosed wherein polyphosphate is included in the gelatin coating, thereby improving gel firmness, adhesive strength and tack.

(Problems to be solved by the invention)

The aforementioned conventional capsule preparation employs synthetic preservatives or petroleum-based agents, and so has the disadvantage that the intrinsic capacities of the capsule preparation are not fully maintained.

In particular, present-day cultural trends place an emphasis on health and natural products, and concern and unease regarding synthetic preservatives (synthetic additives) are increasing. In the fields of cosmetics and foodstuffs, there is particularly high concern regarding synthetic preservatives, and the use of such substances is not in line with the demands of present-day society in which legal restrictions regarding these substances are becoming increasingly stringent.

The object of the present invention, in light of this state of affairs, is to offer a capsule coating composition with anti-spoiling and flavoring characteristics obtained through the use of natural plant extracts, without using synthetic preservatives.

Specifically, by blending plant extracts having anti-spoiling properties and flavoring in the capsule coating agent, this flavoring can be perceived, thus allowing freedom in design of the form of the capsule preparation, and thereby lending to the production of an interesting external appearance. Moreover, when the capsule preparation is placed in the mouth, the capsule will dissolve or disintegrate within a few tens of seconds, thus providing the pleasant taste of the refreshing plant extract.

(Means for solving the problems)

With the aim of overcoming these current problems, the inventors of the present invention arrived at the present invention as a result various investigations concerning plant extracts that have multiple functions related to improving sensation during use and providing preservative/stabilization properties without using synthetic preservatives or petroleum-based resins.

The invention is a capsule coating composition, in which an extract produced by extraction from a plant of the Perilla family is the essential component in the plant extract that is contained in the aforementioned capsule coating composition.

There have been many reports regarding the anti-spoiling and antimicrobial action in plants. Among plants, those that contain thymol, menthol, eugenol an other such antimicrobial and anti-spoiling substances are known to have anti-spoiling and antimicrobial actions that are as high as those of carbolic acid [phenol] systems (the germicidal power of a germicide is determined taking the germicidal power of phenol as 1).

For example, the antimicrobial properties of plants have been reported by Ueda et al. (Foodstuff Technology Society Journal, 29(7) p. 390, 1982).

Examples that can be cited include clove and eucalyptus of the Myrtaceae family, laurel and cinnamon of the Lauraceae family, anise, caraway, coriander, cumin, dill and Ligusticum wallichii of the Apiaceae family, honeysuckle of the Caprifoliaceae family, garlic of the Liliaceae family, or hinoki of the Cuppressaceae family.

In addition, herbal medicines, Western medicinal herbs, folk remedies and materials used as foodstuffs can also be used without particular restrictions, provided that they are plants that have antimicrobial and anti-spoiling action.

It is also possible to use these plants together with materials that have superior flavoring, anti-spoiling and antimicrobial actions. The amounts of these plants blended with a plant of the Perilla family has no particular restrictions.

The plant extract used in the present invention has no particular restrictions, and can be an extract of plants of the Perilla family used in herbal medicine, Western medicinal herbs, folk remedies, or substances used for foodstuffs. Examples of plants of the Perilla family include thyme, sage, rosemary, oregano, marjoram, lavender and savory, with thyme, sage, and rosemary being preferred, because they have long been used for their anti-spoiling action.

When plants of the Perilla family are used individually, or when plants of the Perilla family are used in combination, it will be possible to obtain sufficient anti-spoiling properties or flavoring properties [sic; corrected in Procedural Corrections section].

Because a plant extract is added to the capsule coating composition, each of the plants is extracted with a solvent that is appropriate for its target, and the plant extract subsequently obtained by filtration, concentration and separatory processes is then blended with the capsule coating agent. Examples of solvents for extracting the anti-spoiling components or flavoring components that may be cited include water, ethanol, methanol and other hydrophilic solvents, and ether, chloroform, ethyl acetate and other hydrophobic solvents. By selecting solvents that are appropriate for a given plant, the effective component can be extracted. Preferred solvents that are used in this case are water, ethanol, and ethanol/water systems, with a 30-90% ethanol/water system solvent being particularly desirable.

The plants used in order to obtain a plant extract can be fresh or dried, and can be used without particular restrictions.

The amount of extraction solvent will differ depending on the type of plant, but is generally about 1/10 to 40/1 in terms of the plant ratio with respect to the solvent.

The extraction method can involve cold infusion or hot infusion, and in general, infusion is performed for a few hours to a few days at room temperature to 90°C.

The crude plant extract obtained in this manner can then be filtered, washed, concentrated, subjected to chromatography using silica gel or other carrier, or subjected to vapor distillation in order to separate the effective components having anti-spoiling, antimicrobial, or flavoring properties. It is preferable to use the extract after having removed as much of the other components as possible.

The extract concentration of the plant extract is taken as the minimum concentration required for production of the capsule coating composition, and thus can be adjusted so that the content of effective component is increased.

In blending the capsule coating agent and plant extract, plants of the Perilla family have strong anti-spoiling effects, and so it is necessary to blend one or more types of extract from plants of the Perilla family. However, it is difficult to combine plants of the Perilla family to obtain both anti-spoiling effects and flavoring properties, and so it is necessary to add plant extracts from plants other than those of the Perilla family.

The blend amount of plant extract in the capsule base is in a range that allows maintenance of proper strength and moisture absorption properties of the final capsule formulation. If the anti-spoiling effects are insufficient, or if the drug odor is too strong, this will present problems from a practical standpoint. Thus, the extract must be used in an amount whereby the functionality is maintained in regard to the required anti-spoiling effects, aroma and flavor.

The blend amount of plant extract with respect to capsule base will be different depending on the type and concentration of the plant extract, but an amount in the range of a weight ratio of 2-40% with respect to the capsule base is generally appropriate. At less than 2 wt%, the anti-spoiling effects and aroma will be insufficient, whereas an amount that is greater than 40 wt% will cause problems in terms of maintaining the physical properties of the capsule coating composition.

Commonly used substances can be used for the capsule coating agent without particular restrictions. Examples that can be cited include gelatin, shellac, xanthan gum, pullulan, dextrin, guar gum, carrageenan, pectin, agar, alginate and cellulose derivatives. These capsule coating agents can be used individually, or multiple types can be used in combination.

The concentration can be adjusted using water, plant extract or other blending agents so that the capsule coating base dissolution concentration is 30% or greater, thereby allowing dissolution of the capsule coating agent. A sheet is formed from the capsule coating solution, and said sheet is then heated to above its fusion point, whereupon the material is stamped into the form of depressions, and a pair of stamped depressions is fused and dried to produce the capsule preparation.

The capsule preparation can be completely dried to eliminate water content, or can have the form of a soft capsule in which some water content is allowed to remain to impart softness. The water content remaining in the capsule base is preferably 50% or less. If this amount is greater than 50%, then moisture absorption will be too high, leading to an undesirable drop in storage stability. It is preferable for the residual water content in the soft capsule preparation to be 10-40%.

In an additional preparation method used in the present invention, the capsule base can be dispersed in plant extract, and wetted therewith to produce a viscous solution,

which is then deaired. While hot, an applicator can be used in order to adjust the thickness, whereupon the material is extruded from a slit and drawn to produce a sheet (ribbon) material with a constant thickness. Subsequently, the material can be allowed to cool while supplying dry air, thereby producing a sheet of uniform thickness. This sheet (ribbon) can also be produced by blending in a third component. In this case, the third component can be added to the aforementioned heated solution, or the third component can be coated, infused or laminated with respect to the resulting sheet (ribbon). Examples of third components that can be cited include colorants, flavorings and fillers.

The stamped capsule base is then molded into various shapes after the inside is filled with the prescribed medicinal components, dissolution conditioners, flavorings and other suitable materials. Liquid materials are preferably used for the filling content, but when the content is powder, it can be loaded in the form of a dispersed suspension. The loading method involves employing conventional capsule preparation manufacturing methods in order to manufacture the preparation. For example, a dipping method, stamping method (rotary die method, *akojieru*[*] method, etc.) or dripping method can be cited.

Drying of the capsule preparation after its filling has been introduced is carried out at a temperature at which the contents are not modified, and absorption of moisture by the gel base is not induced.

The present invention is described in additional detail below by providing working examples.

Working examples

Preparation of plant extract

- Extraction example 1

1000 mL of aqueous 35% ethanol solution were added to 100 g of thyme, and the thyme was extracted while heating for 24 h. The solvent was then evaporated off from the extract at low temperature to obtain crude thyme extract with a light-reddish brown color. This crude extract was then redissolved in 250 mL of aqueous 60% ethanol solution, and the insoluble matter was removed by filtration to obtain 205 mL of thyme extract. This extract was used in the manufacture of the capsule coating agent.

- Extraction Example 2

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[*] phonetic spelling—Trans. Note.

100 g of raw rosemary were subjected to the same extraction method as in Extraction Example 1 above to obtain 200 mL of rosemary extract.

- Extraction Example 3

100 g of raw sage were subjected to the same extraction method as in Extraction Example 1 above to obtain 210 mL of sage extract.

- Extraction Example 4

100 g of raw eucalyptus leaves were subjected to extraction by the same method as in Extraction Example 1 above, to obtain 205 mL of eucalyptus extract.

- Extraction Example 5

100 g of dried tansy were subjected to extraction by the same method as in Extraction Example 1 above to obtain 210 mL of tansy extract.

Extraction Example 6

100 g of raw hinoki were subjected to extraction by the same method as in Extraction Example 1 above, to obtain crude hinoki extract. This crude hinoki extract was subjected to steam distillation to obtain 16.8 g of hinoki extract.

Next, the capsule compositions were prepared as presented in the working examples.

Working Example 1

100 g of purified gelatin, 50 parts of purified water and 20 parts of sorbitol were admixed, and water absorption and swelling were allowed to occur. The mixture was then heated to 80°C and the materials were uniformly dissolved to obtain a first solution.

Next, 12 parts of thyme extract, 4 parts of sage extract, 1 part of eucalyptus extract and 60 parts of purified water were added to 15 parts of pullulan, and the mixture was heated to bring about dissolution. The above dissolved gelatin solution was then maintained at 60°C while stirring, and the pullulan solution was added in small amounts to produce a uniform transparent capsule coating agent.

Vitamin E was used as the content for the capsule preparation, and a soft capsule preparation was obtained by a rotary stamping method. The content weight of the soft gel capsules was 250 mg, and the capsule coating preparation weight was 130 mg.

Working Example 2

100 parts of gelatin, 70 parts of purified water and 15 parts of sorbitol were admixed in order to allow water absorption and swelling. The mixture was then dissolved until uniform at 80°C. 20 parts of hydroxypropyl methylcellulose phthalate were then dissolved in 12 mL of 0.1 N sodium hydroxide solution, and the following were added to this viscous solution: 13 parts of thyme extract, 8 parts of rosemary extract, 4 parts of sage extract, 0.2 part of hinoki extract and 60 parts of purified water, whereupon the mixture was dissolved until a uniform solution was obtained. The previously dissolved gelatin solution was then maintained at 60°C while stirring, and the pullulan solution was added in small amounts to obtain a uniform transparent capsule coating agent solution. Subsequently, a soft capsule preparation was obtained in the same manner as in Working Example 1.

Working Example 3

100 parts of purified gelatin, 60 parts of purified water and 25 parts of sorbitol were admixed in order to allow water absorption and swelling, and the mixture was then dissolved until uniform at 85°C. To 15 parts of dextrin were added 10 parts of rosemary extract, 6 parts of tansy extract, 2 parts of eucalyptus extract, 0.1 part of hinoki extract and 40 parts of purified water, and the mixture was dissolved until uniform. The previously dissolved gelatin solution was then maintained at 60°C while stirring, and the dextrin solution was added in small amounts to obtain a uniform transparent capsule coating agent solution.

A soft capsule preparation was obtained in the same manner as in Working Example 1.

Comparative Example 1

0.3 part of ethyl paraben (parahydroxybenzoic acid ethyl ester), 0.1 part of methyl paraben (parahydroxybenzoic acid methyl ester), 20 parts of xylitol, 5 parts of sodium polyphosphate and 70 parts of purified water were admixed and dissolved, and 100 parts of purified gelatin were added to this in order to allow water absorption and swelling. The mixture was then dissolved until a uniform solution was obtained at 60°C. Subsequently a soft capsule preparation was obtained in the same manner as in Working Example 1.

Comparative Example 2

100 parts of purified gelatin, 85 parts of purified water and 25 parts of sorbitol were admixed in order to allow water absorption and swelling, and the mixture was then

dissolved until a uniform solution was obtained at 60°C. Subsequently, a soft capsule preparation was obtained in the same manner as in Working Example 1.

Investigations were then carried out regarding the storage stability of the capsule preparations manufactured in this manner. Specifically, the capsule preparations obtained in Working Examples 1-4 and Comparative Examples 1 and 2 were introduced into a sealed container, and were left inside on a shelf for 30 days, or were left for 30 days under conditions of 40°C and 75% relative humidity (RH). The results are presented in Table 1.

The capsule preparations produced in Working Examples 1, 2 and 3 and Comparative Examples 1 and 2 were then subjected to testing of flavoring (perceptual) using panelists. The results are presented in Table 2.

The capsule preparations obtained in Working Examples 1, 2 and 3 and Comparative Examples 1 and 2 were also subjected to a spoiling resistance test. The results are presented in Table 3.

Effect of the invention

With the capsule coating composition described in detail above, extracts from natural plants are contained in a capsule coating agent without the use of any synthetic preservatives or flavorings. By this means, spoiling resistance and flavoring can be imparted with sufficient effect, thus allowing preservation of stability over long periods of time.

In addition, a capsule coating composition that provides a refreshing sensation and is well perceived during use can be provided, because the capsule preparation contains blended plant extracts, and the capsule dissolves or disintegrates in the mouth over a period of a few tens of seconds.

Applicant: Kotobuki Academy K.K.
Agent: Takashi Miyara, Patent Attorney (and 1 other)

Table 1 Effects during storage stability testing

Test product type	Room temperature, 30 days	40°C, 75% RH, 30 days
Working Example 1	No change	No change
Working Example 2	No change	Slight swelling
Working Example 3	No change	No change
Comparative Example 1	No change	No change
Comparative Example 2	No change	No change

Table 2 Effect of testing for flavoring (units: number of panelists)

Test product type	Senstation during use			Flavoring		
	0 points	1 point	2 points	0 points	1 point	2 points
Working Example 1	0	6	10	0	5	11
Working Example 2	0	7	9	0	4	12
Working Example 3	0	6	10	0	4	12
Comparative Example 1	4	11	1	6	10	0
Comparative Example 2	10	6	0	9	7	0

Note 1: Number of panelists: 16

Note 2: Evaluation standards

2 points: Very good

1 point: Good

0 points: Not good

Table 3. Spoiling/antimicrobial testing

Test product type	Colony growth inhibition (%)	
	E. coli	Aspergillus niger
Working Example 1	69	71
Working Example 2	75	72
Working Example 3	71	74
Comparative Example 1	82	84
Comparative Example 2	7	9

Note 1: Microorganism culturing conditions;

- E. coli (Escherichia coli IF0-3972)

One platinum loop of bacterial solution at 1.5×10^9 cells/mL (approximately 0.02 mL) is used in order to streak normal agar plate medium in culture dishes of 105 mm diameter, and capsules are placed in 4 locations thereupon. The plates are then cultured for 3 days at 25°C.

- A. niger (Aspergillus niger ATCC-6272)

One platinum loop of yeast solution at 7.9×10^6 cells/mL (approximately 0.02 mL) is used in order to streak potato agar plate medium in culture dishes of 105 mm diameter, and capsules are placed in 4 locations thereupon. The plates are then cultured for 2 weeks at 25°C.

Note 2: Inhibition (%) = $\frac{\text{(Surface area with no microorganism growth)}}{\text{(Surface area of plate)}} x100$

Procedural Corrections (Voluntary)

August [illegible], 1989

Patent Office Commissioner: Fumiki Yoshida

1. Document:

Heisei 1 (1989), Patent Application No. 147512

2. Title of the invention:

Capsule Coating Composition

3. Person making corrections:

Relationship to Document: Patent Applicant

Address:

Name: Kotobuki Academy K.K.

4. Representative: T 730 082-221-3901

Address: 13-14 Nobori-machi, Naka-ku, Hiroshima-shi,
Shin-Hiroshima Bldg. 9th floor

Name: Masao Miyake (4224), Patent Attorney (and 1 other)

5. Date Correction Ordered: Voluntary

6. Number of inventions added due to correction: 0

7. Subject of correction: Specification, Table 1, Table 2, Table 3

8. Content of correction:

See attached pages Format Inspected

[The remainder of the document is identical to the first part, with the exception of the passages indicated below.]

(Means for solving the problems)

1 With the aim of overcoming these current problems, the inventors of the present invention arrived at the present invention as a result various investigations concerning plant extracts that have multiple functions related to improving sensation during use and providing preservative/stabilization properties without using synthetic preservatives or petroleum-based resins.

2 The invention is a capsule coating composition, in which an extract produced by extraction from plant of the Perilla family is the essential component in the plant extract that is contained in the aforementioned capsule coating composition.

3 There have been many reports regarding the anti-spoiling and antimicrobial action in plants. Among plants, those that contain thymol, menthol, eugenol and other such antimicrobial and anti-spoiling substances are known to have anti-spoiling and antimicrobial actions that are as high as those of carbolic acid [phenol] systems (the germicidal power of a germicide is determined taking the germicidal power of phenol as 1).

4 For example, the antimicrobial properties of plants have been reported by Ueda et al. (Foodstuff Technology Society Journal, 29(7) p. 390, 1982).

8 The plant extract used in the present invention has no particular restrictions, and can be an extract of plants of the Perilla family used in herbal medicine, Western medicinal herbs, folk remedies, or substances used for foodstuffs. Examples of plants of the Perilla family include thyme, sage, rosemary, oregano, marjoram, lavender and savory, with thyme, sage, and rosemary being preferred, because they have long been used for their anti-spoiling action.

6 In addition, herbal medicines, Western medicinal herbs, folk remedies and materials used as foodstuffs can also be used without particular restrictions, provided that they are plants that have antimicrobial and anti-spoiling action.

5 Examples that can be cited include clove and eucalyptus of the Myrtaceae family, laurel and cinnamon of the Lauraceae family, anise, caraway, coriander, cumin, dill and Ligusticum wallichii of the Apiaceae family, honeysuckle of the Caprifoliaceae family, garlic of the Liliaceae family, chamomile, tansy and wormwood of the Asteraceae family, or hinoki of the Cupressaceae family.

7 It is also possible to use these plants together with materials that have superior flavoring, anti-spoiling and antimicrobial actions. The amounts of these plants blended with plants of the Perilla family have no particular restrictions.

9 When plants of the Perilla family are used individually, or when plants of the Perilla family are used in combination, it will not be possible to obtain sufficient anti-spoiling properties and flavoring properties.